Enteric Diseases and Antimicrobial Resistance
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Based on the FoodNet 1996-1997 study and other sources, the Centers for Disease Control and Prevention (CDC) estimated 211 million acute gastroenteritis, resulting in 900,000 hospitalizations, and over 6,000 deaths each year in the United States. Among the gastroenteritis, foodborne illness was a significant attribution. It is estimated that 76 million of foodborne illesses, 323,000 hospitalizations and 5,200 deaths each year (Mead et al. 1999). Over 90% of foodborne illnesses are caused by microorganisms. Among the bacterial agents, *Campylobacter* and *Salmonella* account for the greatest number of both estimated and reported causes of foodborne disease, followed by *Clostridium perfringens, Staphylococcus aureus*, various *Escherichia coli* pathotypes, *Shigella* spp., and *Listeria monocytogenes.* Studies have shown that antimicrobial-resistant non-typhoidal *Salmonella* causes treatment failures, complications, increased virulence, elimination of competing intestinal flora, pathogen overgrowth, increased likelihood of hospitalization, longer hospitalization, and an increased likelihood of death.

In 1996, the National Antimicrobial Resistance Monitoring System (NARMS) was launched as a collaborative effort among the Food and Drug Administration, CDC, and the U.S. Department of Agriculture, to document the emergence of antimicrobial resistant pathogens in the United States. A study by NARMS in 2002-3 showed that multi-drug resistance was widespread in *Salmonella* strains isolated from food animals on the farm, and raw retail meats. Without question, the transmission of antimicrobial-resistant pathogens from animal husbandry and the environment to humans represents a complex phenomenon, involving the management of human sewage, animal manure, clinical waste, and the disposal or recycling of other farm and slaughterhouse-derived material of animal origin. The role of therapeutic and sub-therapeutic use of antimicrobials as well as the use for growth promotion in the emergence and transmission of antimicrobial-resistant pathogens to humans has been described in detail as an unfolding public health concern. One example described the introduction and dissemination of streptothricin resistance in the former East Germany. When introduced on the farm to treat pigs in 1982, there was no streptothricin resistance noted in the animal or human microbial flora. By 1983 resistance was detected among *E. coli* strains isolated from pigs and in farm personnel. By 1984 resistance had spread to farm families, and in 1985 was found in the community in the form of streptothricin-resistant *E. coli* and as drug-resistant urinary tract infections. Lastly, in 1987 streptothricin resistance was found in the closely-related enterobacteriaceae *Shigella sonnei.*

Much evidence shows that removal of specific antimicrobials from the agricultural arena leads only to a slow diminution of resistance; that drug resistance is the rule, and not the exception; and that resistance increases from low levels to high levels, through an intermediate stage. This was seen with beta-lactam resistance in *Streptococcus pneumoniae*, and fluoroquinlone resistance in *E. coli*. In addition, the acquisition of resistance by one antimicrobial commonly expedites the acquisition of additional resistance genes.

Clearly, treatment of chronic enteric infection and re-infection with antibiotic-resistant organisms cannot represent a successful long-term strategy in the face of the rapid development of resistance, and the inevitable decrease in intestinal fortitude caused by unbalancing the normal protective intestinal flora. Furthermore, the timeline for antimicrobial drug development from discovery to product launch is approximately 9.5 years, which compares unfavorably to a few months or a year that it takes after launch for the first examples of resistance to be seen in human clinical isolates. In the likely absence of 'prudent guidelines' or more determined efforts, the problems of antimicrobial resistance will inevitably lead to further dissemination of incurable infections.

- RESEARCH NEEDS:
  - Improved surveillance of susceptibility and resistance is needed both nationally and internationally. Very little is known about the role of international policies and the global spread of resistance from countries with liberal animal husbandry or prescription policies, to countries with more restrictive policies.
  - Research into novel approaches to the development of antimicrobial compounds that elude resistance is urgently needed
  - Improvements in administration are needed, such as short-term, narrow spectrum, high dose therapy
  - Increased education on appropriate use is needed for physicians, veterinarians, clinical labs, agricultural producers, pharmaceutical companies, and policy makers worldwide.